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14. ABSTRACT

The goal of this exploratory project was to demonstrate the feasibility of MR (magnetic resonance) detection of thermoelastically generated tissue motion resulting from localized absorption of pulsed microwave power. All of the instrumentation and software control necessary to deliver high power (4 KW) short-duration (1•s) pulses of continuous 434 MHz RF power synchronized to the MR repetition rate (TR) of the acquisition sequence has been realized. Phantom studies consisting of local absorbers with biologically relevant electromagnetic properties and contrast have been completed which illustrate that displacements of 1-2•m can be generated from the absorption of the pulsed microwave power. MR detection of this small amplitude motion is also evident, although recordings are not sufficiently robust at present because the background motion caused by the natural vibrations of the scanner is much larger creating clutter which makes the microwave induced displacements difficult to detect because they are very near the noise floor of the MR measurement scheme used.

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INTRODUCTION:

The purpose of this project was to explore the feasibility of detection of thermoelastic wave propagation at low frequencies (below 1KHz) induced by preferential microwave energy absorption. Breast cancers are believed to have increased electrical conductivity over that of the normal breast and possibly over that of other pathological but benign processes. Thermoelastic wave propagation generated by high-power microwave absorption has been detected in phantoms and in the human breast at acoustic frequencies (500 KHz–2 MHz) using ultrasound transducers [1-4]. Similarly, ultrasound wave propagation has been detected with magnetic resonance (MR) techniques at very high (relative to diagnostic levels) ultrasound power levels [5]. The feasibility of detecting low frequency displacements with MR when generated by microwave absorption has not been previously considered. If such a signal could be shown to exist and to be reliably detected with MR, it could form the basis for a novel imaging technique with potentially very high contrast and specificity for breast cancer. The goals of the project were to develop the microwave and MR driving and detection subsystems (hardware and software) necessary to test the hypothesis that an MR-detectable thermoelastic displacement wave exists at low frequencies when biological phantoms are exposed to pulsed microwave power. We termed the imaging technique Magnetic Resonance Microwave Absorption imaging or MRMA in short.

BODY:

The research completed as part of this project developed the necessary hardware and software to deliver very short-duration high-powered microwave pulses to a phantom with biological properties and to detect the response with MR based on phase contrast acquisition sequences synchronized to the microwave power pulse train. In the subsections below, we describe the progress achieved in realizing this system and the outcomes from experiments completed during the funding period. It is important to recognize that this project was an exploratory effort with high risk but potentially high gain as well. Its complexity resulted from the fact that the studies were focused on determining whether a signal exists (or not) while also having to develop new delivery and detection subsystems that were unproven. As a result, interpretation of the findings was particularly challenging because the sources of error associated with a lack of signal could reside in an improperly functioning hardware system, in the characteristics of the signal generation or its detection or the fact that the signal to be detected does not physically exist at a level which can be measured with the MR.

System Development: There are two aspects to the system development that are closely linked: (1) microwave power delivery and (2) MR signal detection. The following subsections detail the progress achieved in each of these areas.

(1) Microwave illumination: We designed and constructed a waveguide illuminator capable of radiating short-duration bursts of continuous 434 MHz high-power (up to 10 KW) signals. The antenna was attached and sealed to a plexiglas box for use in phantom experiments. Figure 1 shows a photograph of the unit. The box dimensions are 30 (L) x 15 (W) x 15 (H) cm and the radiating front-face of the waveguide is 5.4 x 2.7 cm. Phantom materials, typically saline with varying amounts of NaCL concentration, are placed in the box and localized inclusions (typically gels of variable salinity in high contrast with the electromagnetic loss in the background) are suspended in various positions relative to the waveguide. This system has proved to be an effective design for conducting the phantom studies described below in terms of its practical functionality and technical performance.

Figure 1: Waveguide radiator attached to a phantom box used for MRMA experiments.

(2) MR signal detection: The second critical component of system development is the hardware and software control associated with the microwave power delivery. Figure 2 presents a system diagram and signal timing sketches for the method we have developed. The function generator receives a trigger signal every 20 ms from the MR scanner and produced a square wave output with a controllable duty cycle. In the testing experiments summarized here, a pulse with 1μs duration (0.005% duty cycle) has been created and sent to a switch. The signal generator communicates a continuous 434 MHz low (2mW) amplitude sine wave to the switch as well which multiplies the two inputs and sends the output to a power amplifier. A portion of the amplified signal is sampled and recorded by a spectrum analyzer while the rest of the signal is connected to the waveguide radiator in Figure 1. Figure 3 shows photographs are various components of the hardware system diagramed in Figure 2. Time-domain traces of the output of the switch created by the MR with a prototype pulse sequence

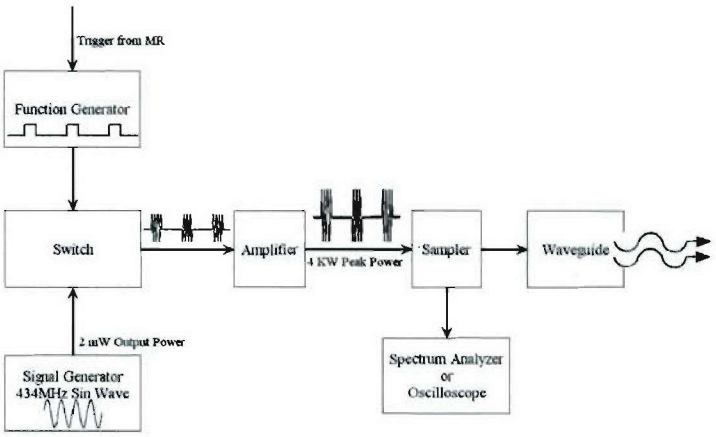

Figure 2: MRMA system diagram and signal timing sketch.

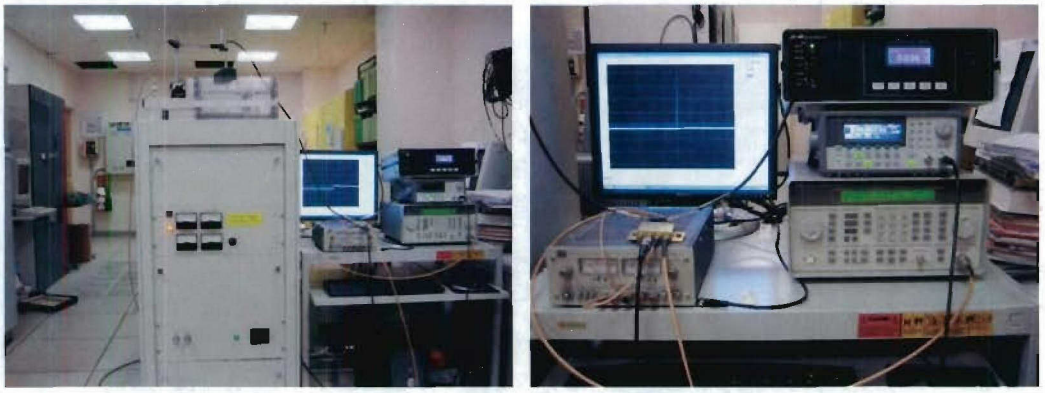

Figure 3: Photographs of the microwave pulsed-power delivery system. Left view shows the microwave amplifier and the associated signal control system for MR synchronization. Right picture is a close-up view of the signal control system and test equipment including the function and signal generators, power supply and signal measurement units.

which illustrates that the system successfully generates the necessary driving signals for synchronizing the microwave power pulses with the MR motion encoding are displayed in Figure 4. Measurements have also been made after amplification as illustrated in Figure 4 where it is evident that the synchronous repetition of very short duration, high-amplitude pulses are being delivered to the waveguide. The temporally magnified view shows that the envelop of the burst signal has excellent rise-time characteristics and is not contaminated with noise or leading/trailing edge ringing.

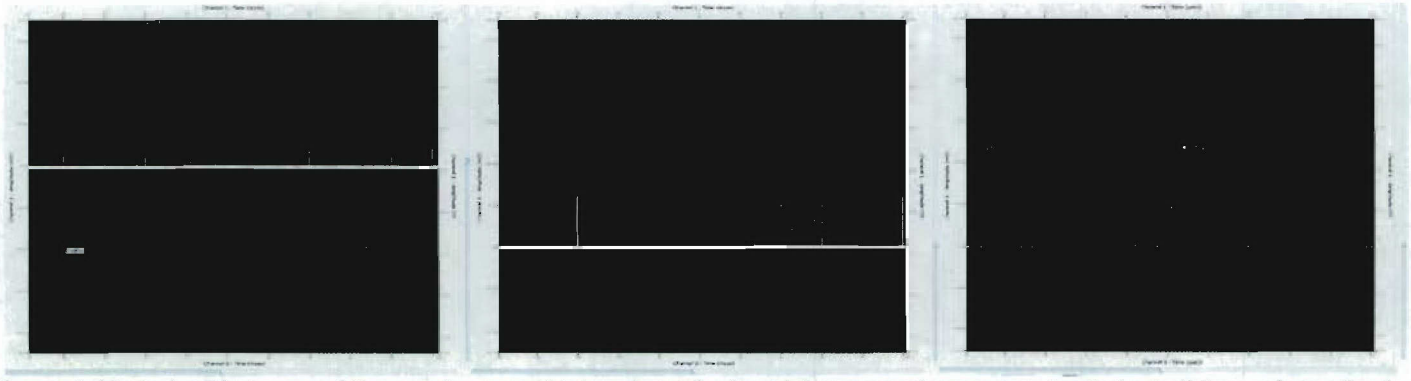

Figure 4: Time-domain traces of the synchronous driving signal for the high-power microwave pulse train. Left trace shows the 1μs duration output pulses of the switching system triggered by the MR every 20 ms to feed a 434 MHz sinusoid to the power amplifier. Middle trace is the signal envelop after power amplification. Right trace is a temporally magnified view of a single amplified pulse.

Pulse Programming: We have completed all of the necessary pulse programming to control the system and concomitant motion encoding from the MR console. We use a file system resident on a linked but separate computer to distribute the function generator commands necessary to execute the synchronous driving signals provided through the system diagram in Figure 2. Here, we have full flexibility in terms of setting the pulse duration, repetition rate and phase offset depending on the selected MR parameters for the acquisition sequence. Developing this flexibility was nontrivial and created a number of difficulties that required persistence to overcome. For example, controlling the phase offset of the microwave pulse relative to the start of each repetition is fundamental to the acquisition. The phase offset is adjusted at the end of a full complement of phase encodes for an image. A 2-second rest period was introduced between the phase offset changes to accommodate the necessary communications between the MR, the linked system control computer and signal generator. Initially, we completed the necessary control software but found that the microwave amplifier continued to produce an output signal during the rest cycle. The problem was difficult to diagnose because it occurred infrequently and seemingly irregularly and for short durations during which we found unexplained and erratic overall system behavior (which we later traced to the root of the problem). After extensive testing and signal tracing during, we finally determined that we had to explicitly turn off the signal generator output because when it switched out of the triggered mode, it defaulted to a constant output at the last level of the truncated sine wave that was capable of triggering the switch depending on its amplitude. While certain difficulties arose, we were able to resolve all of the software timing problems to create a robust acquisition process with parameter control from the MR console. This significantly facilitated the experiments we completed during the project and is a very functional legacy for continued research of the MRMA imaging technique.

Phantom Studies: We completed a large number of phantom studies in an effort to determine whether the MRMA signal exists and whether it can be detected with a conventional clinical scanner (1.5T GE system in this case). There are several dimensions of the problem that we pursued. First, we tried to use the system described in the previous subsections to detect a response in a liquid phantom held in an MR-compatible glass tube suspended within the phantom box filled with water. After a series of experiments conducted over numerous MR imaging sessions we found that vertical displacements were larger in the top and bottom of the glass tube relative to its mid-section (where the waveguide was directed) and that these valves were larger than displacements detected along the axis of the bore of the magnet which were found to be larger on the back side (away from the waveguide face) relative to the front (closer to the waveguide face) of the tube. Figure 5 shows MR images of typical results from these studies. As is evident in the figure, we found the data difficult to interpret because the background motion of the surrounding water was large and the motion in the tube was much smaller and not consistent from experiment-to-experiment. From these investigations we concluded that, although it appears that we have detected a signal

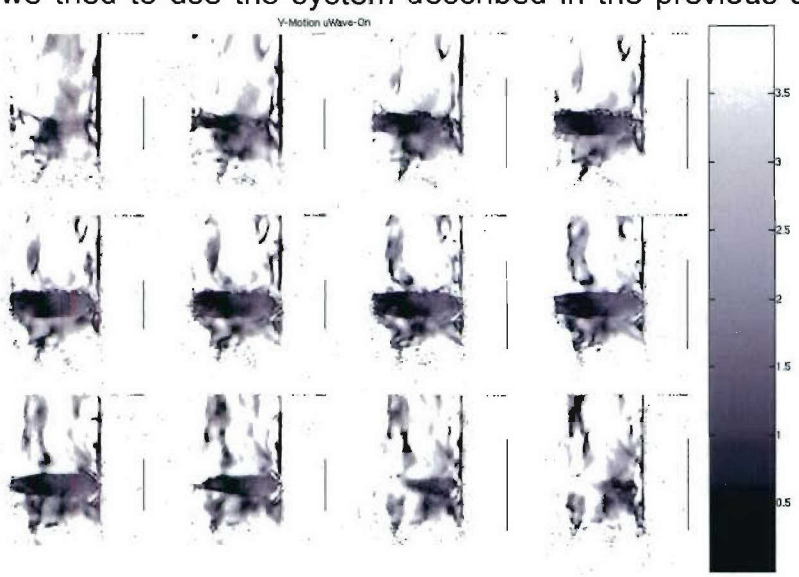

Figure 5: MR motion encoded displacement maps (grayscale in microns) for vertical motion (left-right in the figure) in a phantom exposed to pulsed microwave power. Darker outlines show the MR-compatible test tube representing an inclusion with high absorption properties. The tube was stabilized within the surrounding water in the phantom box which was free to move with the background vibrations of the scanner. The vertical motion in the tube appears to be generated by the microwave absorption and was larger in this direction (as expected) relative to that along the other axes of the tube, although the displacements are small (1-2 microns) and near the noise floor of the MR measurements.

generated by physical motion, more controlled study (and validation) of the actual displacements being produced by the microwave power absorption was warranted. We also felt that it was critical to document the localized absorption of the microwave power and to optimize its deposition in order to maximize the displacement effect.

In a first series of experiments we measured the electric field in the phantom box with and without an inclusion. We found a persistent standing wave pattern as illustrated in Figure 6 which was not strongly influenced by the presence of the inclusion. This allowed us to locate the inclusion in a zone of maximum field strength in order to increase the absorbed power. We then conducted a number of temperature-rise experiments in order to determine the parameters that appear to optimize the microwave power absorption. We used temperature rise as a surrogate indicator of the power absorption that could be easily measured with readily available instrumentation. The test set-up proved to be very informative. For example, we found that we could localize the maximum temperature rise in either the front or back portion of the inclusion depending on its placement relative to the peak of the standing wave pattern in Figure 6. We showed increases in temperature rise with increases in the conductivity of the inclusion and increases in the duty cycle of the microwave power during each MR repetition (TR). While these results are expected, they were gratifying because they demonstrated that we had gained a degree of control over the microwave power deposition process.

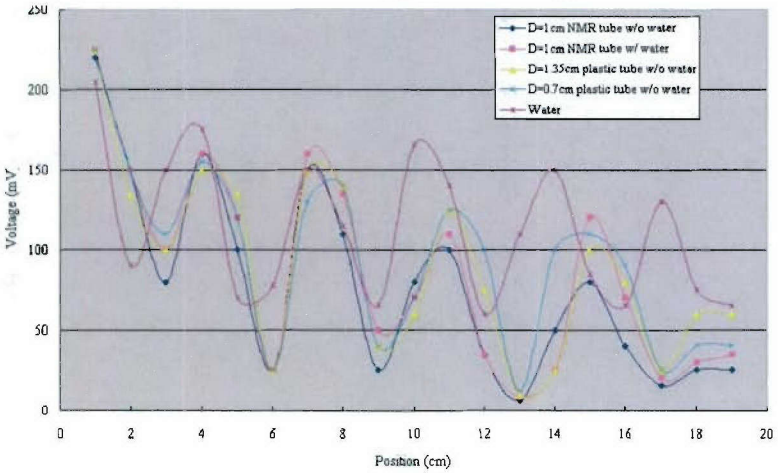

Figure 6: Electric field measurements as a function of distance from the radiating face of the waveguide showing the standing wave pattern that develops in the phantom box. The pattern is relatively insensitive to the inclusion size and composition. Measurements in the presence of both MR-compatible glass test tubes and plastic tubes of different diameters filled with and without water are shown

The study consisted of 9 inclusions that were divided into 2 groups for comparison. The first 3 inclusions were placed in 2 different sized MR-compatible glass test tubes with diameters of 0.5 and 1 cm. The remaining 6 inclusions were put in 4 different sized plastic tubes with diameters of 0.7, 1.35, 2.0 and 2.77 cm, respectively. The plastic tubes had three cut-out windows wrapped with thin polyethylene to improve the RF absorption. Inclusions were placed in the phantom tank and exposed to microwave radiation with 4KW peak power with a 2.5% duty cycle for 5 minutes in concert with the MR driving signals to be expected during an exposure experiment. Figure 7 shows typical results from the study.

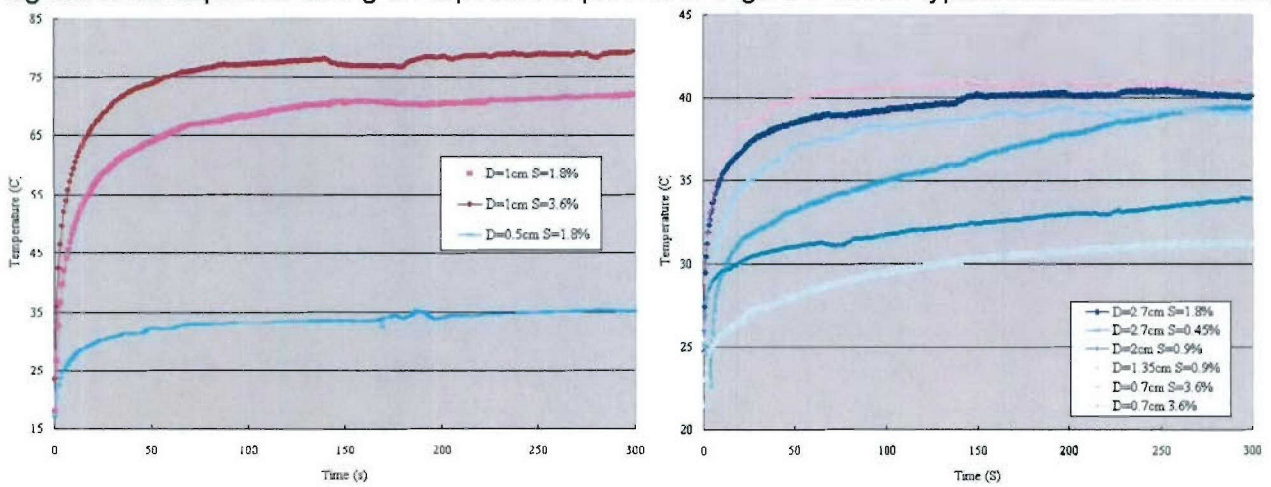

Figure 7: Temperature elevations from exposure to high-intensity short-duration pulsed microwave power where the size and salinity of the absorber was varied. Salinity was the most important factor in making the inclusions more absorptive, although use of the MR-compatible glass tubes was also critical. The initial rate of temperature rise is proportional to power deposition.

We found the temperature rise to be largest in the MR compatible test tube relative to the plastic tubes, larger diameter inclusions absorbed more power than their smaller diameter counterparts (at the same salinity) but higher saline concentration was the most important factor in making the inclusions more absorptive. We also concluded that the response time of the thermal sensors was insufficient to evaluate the transient behavior of the power absorption in order to infer the size of the actual displacements induced.

To directly measure the size of the microwave induced displacement, we developed a measurement scheme based on an optical sensor. Figure 8 shows a typical result for a gel inclusion doped with 1.8% saline placed in the 1 cm MR-compatible test tube. The microwave heating pulses were 4KW peak power with a pulse width of 0.5μs and a repetition rate of 50Hz. The peak-to-peak motion of the gel was estimated to be 1.2μm. By changing the properties of the inclusion to a base material with a larger coefficient of thermal expansion we have been able to demonstrate larger displacements. Figure 8 also shows a typical result for this case which indicates that the displacements are about 2μm peak-to-peak.

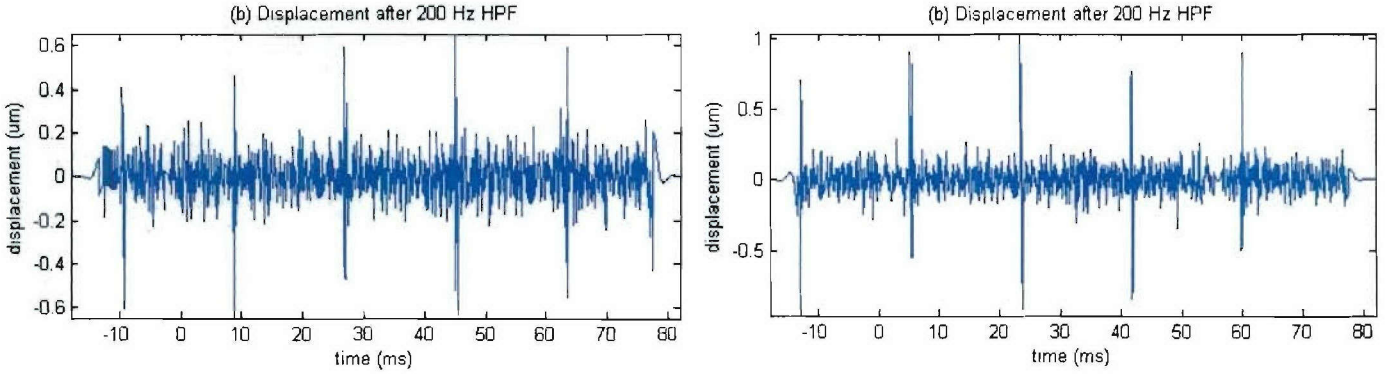

Figure 8: Direct displacement measurements of the motion induced by MRMA in a saline inclusion (left) and a fluid with an increased coefficient of thermal expansion (right). These results show that the displacements induced by the pulsed microwave absorption are in the 1-2μm range peak-to-peak.

KEY RESEARCH ACCOMPLISHMENTS:

- Developed a microwave heating system for high-power, very short duration pulsed emissions.
- Demonstrated pulsed RF power (434 MHz) exposure of a phantom triggered in synchrony with the MR repetition rate (TR) during phase contrast acquisition sequences.
- Developed the pulse programming to control the important parameters of the microwave exposure and acquisition sequence from the MR console.
- Completed phantom studies which determined inclusion characteristics that increased the microwave power absorption including its location, size and material composition.
- Documented, through direct displacement measurements, inclusion motion from the microwave power absorption of 1-2μm peak-to-peak.
- Completed MR acquisition experiments which suggest the detection of a motion signal, although the robustness of the experiment and the reliability of the results warrant further investigation because the amount of motion induced is very near the noise floor of the MR measurement system used.

REPORTABLE OUTCOMES:

- Patent pending on the MRMA concept and technique.
- Funding for continuation of these studies submitted the NIH and awarded in April 2005 (under R21-CA102938-01).

CONCLUSIONS:

We have obtained what appears to be the first direct measurements of the displacements induced by repetitive high-power short duration microwave pulses in biologically relevant absorptive inclusions. The results show magnitudes on the order of 1-2μm. We have also realized all of the necessary hardware, software and parameter control to execute MR experiments designed to detect the motion. The results from the MR detection data are suggestive but still too ambiguous to be certain that the induced response has been reliably detected because the motion is very near the noise floor of the MR measurement technique. Parameters that are important in determining the response are better understood and are now under some control. In effect, the size of the induced displacements needs to be increased, ideally to 10 microns (or more) or the MR sensitivity to smaller motion needs to be improved. We are optimistic that both can be achieved – i.e. the motion can be increased and the MR detection sensitivity can be improved. We are currently working on several ideas in each of these directions. The pilot data that we have summarized in this report has been instrumental in our securing of additional funding from NIH to continue the project.

The concept of MRMA is very exciting because if it can be optimized, it may be a novel approach to exploiting the high contrast in the microwave properties of breast cancers relative to the normal breast on a spatial scale commensurate with MR resolution. This could lead to an entirely new approach for MR breast examination. Based on the studies completed during this exploratory project it is clear that the problem is challenging and more complex than initially realized. However, the overall results are sufficiently encouraging at this stage to warrant further investigation of the process as the basis of an imaging technique for the breast.

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